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EXAMINER	
LEAVITT, MARIA GOMEZ	
ART UNIT	PAPER NUMBER
1633	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/524,945	PARHAMI, FARHAD	
	Examiner	Art Unit	
	MARIA LEAVITT	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-6,8-12 and 15-41* is/are pending in the application.

4a) Of the above claim(s) *4,5,9,10,18,22,27 and 29-41* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3,6,8,11,12,15-17,19-21,23-26 and 28* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *04/01/10;05/20/10*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Detailed Action

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 1, 3-6, 8-12, 15-41 are pending. Claims 2 and 7 have been cancelled and claims 1, 5, 6, 12, 15, 16, 19, 20, 24, 25, 29, 30 and 41 have been amended by Applicants' amendment filed on 04-09-2010. Claims 4, 5, 9, 10, 18, 22 and 27 were previously withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected species, and claims 29-41 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim.

A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Applicants' election without traverse of the species bisphosphonates as the secondary agent reading on claims 23 and 28, in Applicants' response filed on 03-31-2008 was previously acknowledged.

Therefore, claims 1, 3, 6, 8, 11, 12, 15-17, 19-21, 23-26 and 28 are currently under examination to which the following grounds of rejection are applicable.

Response to arguments

Withdrawn objections in response to Applicants' arguments or amendments

Claim objection

In view of Applicants' cancellation of claims 2 and 7, and further in view of Applicants' deletion of the misspelled term "pregnenolone" in claims 16 and 25, objection to claims 2, 7, 16 and 25 is moot.

Notice of Non-Compliant Amendment (37 CFR 1.121)

In view of Applicants' amendment of claim 22 to be identified with the proper status in the claim listing as "withdrawn –Previously presented", objection to the claim 22 as failing to comply with 37 CFR 1.121(c) has been withdrawn.

Claim Rejections - 35 USC § 103(a)

In view of Applicants' amendment of claims 1 and 6 to specifically recite species of oxysterol and the phrase "to induce osteoblastic differentiation and to inhibit adipocyte differentiation of the MSCs" and "a biological marker of osteoblastic differentiation", rejection of **claims 1, 3, 6, 8, 11, 12** under 35 U.S.C. 103(a) as being unpatentable over Paralkar et al., US Publication no. 20040176423 (Date of Publication September 9, 2004), in view of Parish et al., (1995, Lipids, pp. 247-251), and further in view of Wang et al. (Clinical Orthopaedics and Related Research, 2000, 370: 295-310) has been withdrawn.

The combined disclosure of Paralkar, Parish, and Wang fails to teach or suggest a direct correlation between statins' inhibition of HMG Co-A reductase and induction of osteoblastic differentiation. Note that Mundy discloses that

Given the alleged casual connection between lovastatin action and stimulation of osteoblasts differentiation, one of ordinary skill in the art at the time of the invention would not have a reasonable expectation of success in combining these references because the simple substitution of one oxysterol of Parish for the statins of Paralkar would have not yielded predictable results of induction of osteoblastic differentiation and inhibition of adipocyte differentiation of MSCs. Note that Mundy (Science, 1999; page 1946, column 1) demonstrates a casual relationship between the ability to inhibit HMG-CoA reductase activity and their alleged

ability to induce osteoblastic differentiation, particularly because Rao et al., (1999; *Pro. Natl. Aca. Sci.*) discloses an alternative pathway as a target of lovastatin action outside the mevalonate/cholesterol pathway, i.e. a lovastatin independent mevalonate/cholesterol pathway essential for cell division. When no direction as to which of many possible choices is likely to be successful, an invention would not have been obvious to try. Bayer Schering Pharma AG v. Barr Labs. Inc., 91 USPQ2d 1569, 1573 (Fed. Cir. 2009). Accordingly, no *prima facie* case of obviousness exists. Note that claim 6 is generically drawn to a method of stimulating any mammalian cell and not MSCs.

Rejections maintained in response to Applicants' arguments or amendments

Claim Rejections - 35 USC § 103(a)

To the extent that independent claims 15, 19 and 24 are generically drawn to "increasing the number of osteoblasts present in bone tissue", "increasing bone mass" and "ameliorating the symptoms of the osteoporosis", respectively, by the administration of at least one oxysterol, the following rejection stands.

Claims 15-17, 19-21, 23-26 and 28 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Paralkar et al., US Publication no. 20040176423 (Date of Publication September 9, 2004), in view of Parish et al., (1995, Lipids, pp. 247-251) and further in view of Wang et al. (Clinical Orthopaedics and Related Research, 2000, 370: 295-310).

Response to Applicants' arguments as they apply to rejection of 15-17, 19-21, 23-26 and 28 under 35 U.S.C. 103(a)

At pages 9-18 of the remarks filed on 04-09-2010, Applicants essentially argue that: 1) the teachings of Paralkar, itself, are restricted to administering a combination of at least two

compounds, a statin, and a prostaglandin receptor agonist, 2) In fact, nowhere, in the entirety of Paralkar does this reference teach or suggest that administration of statin alone would be useful for enhancing bone formation in a mammal, 3) The Mundy reference and related '779 patent discussed in the Paralkar publication at ¶ [0053] and¶ [0013], respectively of the published application teach that contacting immortalized osteoblasts cell lines (murine 2T3 cells) or human MG-63 osteoblasts with statins results in increase BMP-2 expression, 4) the immortalized osteoblasts cell lines of Mundy are not mammalian mesenchymal stem cells (MSCs), 5) unlike MSCs, the immortalized osteoblasts murine (2T3)cell lines are not multipotent, rather the fate of the murine (2T3) cell lines or MG-63 osteoblasts is already determined to only the osteoblastic lineage, 5) one having skill in the art could only reasonably conclude from Mundy et al., that statins, BMP-2 and FGF have a role in osteoconduction, which takes place after the induction of osteoblastic differentiation (i.e. osteoinduction), 6) there is a logical disconnect to the allegation that oxysterol could substitute for the statins of Mundy, because Mundy demonstrates a casual relationship between the ability to inhibit HMG-CoA reductase activity and their alleged ability to induce osteoblastic differentiation, 7) it would have been unpredictable at the time of filing the present application whether two different inhibitors of HMG-CoA reductase would have the same effect on, e.g., osteoblastic differentiation, 8) HMG-CoA reductase could be eliciting any of a variety of effects on a cell, which might or might not be associated with bone formation or osteogenic differentiation, 9) Mundy teaches that the activity of lovastatin to inhibit HMG-CoA reductase activity to stimulate bone formation by inducing the BMP-2 promoter is casual; 10) the casual relationship means that other agents that inhibit HMG-CoA reductase, such as oxysterols, do not necessarily induce osteoblastic

differentiation, 11) in support of the casual relationship, Mundy states "the increase in luciferase activity was blocked by the immediate downstream metabolite of HMG Co-A reductase, mevalonate, which suggests that the effect on bone formation were causally linked to inhibition of this enzyme [although mevalonate may have cellular effects independent of the cholesterol biosynthesis pathway", 12) indeed, Rao states, "we identified the ubiquitin-proteasome pathway as an alternative, HMG-CoA independent, pathway" ..."these alternative pathways may mediate lovastatin effect on cell proliferation (Rao, page 7797, col. 2, last full paragraph), 13) Wang and colleagues (1995, *J. Formos Med Assoc*, pp. 589-592) fail to teach bone formation in a rabbit model when rabbits were given lovastatin in the absence of steroid treatment, 14) inventors of the 6, 080, 779 patent discussed in the Paralkar publication concludes that "there is not suggestion that lovastatin directly enhances bone formation in the absence of steroid treatment" as no increase in bone mass was seen in chickens administered lovastatin alone compared to control chickens (see Cui et al, *Clin Orthop Relt Res*. 1997, pp:8-19; data presented and discussed by Wang), 15) Wada et al. (2000) Arch. Intern. Med. 160, 2865 reports that the mean bone mineral density was lower in human subjects receiving pravastatin, simvastatin, or fluvastatin than in those not receiving statins, and 16) Parhami et al. (2002) J. Bone Mineral Res. 17, 1997-2003, reports that lovastatin and mevastatin suppressed the expression and activity of alkaline phosphatase and inhibited calcium mineral deposition in pluripotent marrow stromal cells. That is, lovastatin and mevastatin inhibited markers associated with osteogenesis. The above arguments have been fully considered but deemed unpersuasive.

Regarding 1) and 2), Applicants content that Paralkar does not teach or suggest administration of statin alone and appear to infer that administration of statins alone would not

be useful for enhancing bone formation. However, the art as a whole, at the time the invention was made, clearly discloses that statins are HMG-CoA reductase inhibitors, additionally, statins, in particularly lovastatin, simvastatin, mevastatin, and fluvastatin are considered especially useful in that they not only increase the formation of new bone, but also enhance the accumulation of mature osteoblasts, the cells involved in new bone growth (1999, Science, pp. 1946 – 1949). Morever, in preferred embodiments Paralkar teaches administration of pharmaceutical combinations of a prostaglandin agonist and a HMG-CoA reductase inhibitor; however, in nonpreferred embodiments Paralkar discloses:

> "Since the present invention has an aspect that relates to the augmentation of bone growth by treatment with a combination of active ingredients which may be administered separately, the invention also relates to combining separate pharmaceutical compositions in kit form"[emphasis added] ¶ [0088] of the published application.

Disclosed examples and preferred embodiments do not constitute a teaching away from a broader disclosure or nonpreferred embodiments. In re Susi, 440 F.2d 442, 169 USPQ 423 (CCPA 1971). Moreover, case law states that anticipation does not require the actual creation or reduction to practice of the prior art subject matter; anticipation requires only an enabling disclosure. In re Donohue, 766 F.2d 531, 533 [226 USPQ 619] (Fed. Cir. 1985). A reference may enable one of skill in the art to make and use a compound even if the author or inventor did not actually make or reduce to practice that subject matter. Bristol-Myers, 246 F.3d at 1379; see also In re Donohue, 766 F.2d at 533. Thus the Paralkar publication only needs to make one credible assertion of specific utility for the claimed invention to satisfy the 35 U.S.C. 101 and 35 U.S.C. 112; additional statements of utility, even if not "credible," do not render the claimed invention lacking in utility. Thus the claimed invention is anticipated in the description of the Paralkar

publication. As such the description of "administration [of active ingredients] separately" is sufficient to establish inherency.

Regarding 3) and 4), claims 15, 19 and 24 are generically drawn to "increasing the number of osteoblasts present in bone tissue", "increasing bone mass" and "ameliorating the symptoms of the osteoporosis", respectively, by administration of at least one oxysterol. The specification as filed does not provide a closed definition of the phrase "osteoblastic differentiation" but provides markers that are commonly known in the art to identify bone formation such as "increase in alkaline phosphatase activity, calcium incorporation, mineralization or osteocalcin mRNA expression, or other indicators of osteoblastic differentiation" ¶ [0053], of the published application. At the most the specification discloses that alkaline phosphatase activity is an early marker of osteoblastic differentiation ¶ [0079], of the published application. Indeed, the specification as filed evidences osteoblastic differentiation in cultures of MSC by stimulation of alkaline phosphatase activity, osteocalcin gene expression and mineralization of cell colonies are indices of increased differentiation into osteoblast phenotype. However, the specification as filed is silent about any differential markers for detection of osteoinduction versus osteoconduction.

Regarding 5), 6), 7), 8), 9), 10), 11) and 12) Mundy clearly teaches experiments using statins (i.e., inhibitors of HMG-CoA reductase) which induce osteoblastic differentiation by enhanced expression of BMP-2 which is a marker of osteoblasts differentiation and not osteoblast proliferation as FGF (Mundy, Science, 1999; page 1946, column 1). Rao et al,m clearly states that "lovastatin is used for the treatment of hypercholesterolemia because it inhibits HMG Co-A reductase, and thus prevents conversion of HMG Co-A into mevalonic acid". The

examiner agrees that Rao et al., indicates an alternative pathway as a target of lovastatin action outside the mevalonate/cholesterol pathway mediating the effect on cell proliferation. Thus the assertion made by Mundy about the "effects on bone formation were causally linked to inhibition of this enzyme [mevalonate]" refers to stimulation of osteoblastic differentiation. That is why rejection of **claims 1, 3, 6, 8, 11, 12** under 35 U.S.C. 103(a) as being unpatentable over Paralkar et al., Parish et al., and Wang et alhas been withdrawn as the skilled artisan based on the combined evidence of Mundy and Rao would not have had a reasonable expectation of success in inducing osteoblastic differentiation. However, to the extent that the claims 15, 19 and 24 are generically drawn to "increasing the number of osteoblasts present in bone tissue" (i.e. claim 15), "increasing bone mass" (i.e. claim 19) and "ameliorating the symptoms of the osteoporosis" (i.e. claim 24), the fact that there is an alleged casual connection between the inhibitors of HMG Co-A reductase activity and osteoblastic differentiation is not significantly relevant as the claims are not encompassing simultaneously inhibiting adipocyte differentiation and inducing osteoblastic differentiation. Note that Mundy discloses that activation of different pathways resulting in induction of osteoblasts differentiation versus induction of osteoblasts proliferation, which is further supported by teachings of Rao et al., indicating an alternative pathway as a target of lovastatin action outside the mevalonate/cholesterol pathway, said alternative pathway mediating the effect on division and proliferation . Accordingly, activation of any alternative pathway by the statin lovastatin would have been expected to induce each, "increasing the number of osteoblasts present in bone tissue", "increasing bone mass" and "ameliorating the symptoms of the osteoporosis". Furthermore, Garrett et al., summarizes the role of statins at the time the invention was made, enhancing bone formation (Garrett et al., Feb. 2002, *Arthritis Res*, pp. 237-

240). Note that the test for obviousness under 35 U.S.C. 103 requires a highly fact-dependent analysis involving taking the claimed subject matter as a whole and comparing it to the prior art. Like statins, side-chain oxysterols are HMG-CoA reductase inhibitors. Consequently, based on the teachings in the prior art as a whole, one would expect that like statins treatment enhances bone growth and proliferation of osteo-progenitor human cells, side-chain oxysterols would also "increase the number of osteoblasts present in bone tissue", "increasing bone mass" and "ameliorating the symptoms of the osteoporosis".

Regarding 13) and 14), Wang et al., (1995, *J Formos Med Assoc*, pp. 589-92), discloses, "the bone area in the steroid only group was significantly lower than in the groups that have also received lipid clearing agents" (abstract) e.g., lovastatin, clofibrate and bezafibrate. Wang et al., clearly points out that lovastatin is associated with maintenance of bone. Indeed, Fig. 2, at page 591, illustrates how lovastatin alone inhibits HMG-CoA reductase and preserves the bone area (Wang et al., (1995, *J Formos Med Assoc*, p. 591, col. 2, paragraph 3; p 592, col. 1, paragraph 4). Accordingly, lovastatin directly enhances bone formation in the absence of steroid treatment.

Regarding 15), Wada et al (2000, *Arch. Intern. Med.* 160, 2865), the lumbar bone mineral density (BMD) of patients receiving statins was significant lower in Japanese subjects with type 2 diabetes, said subjects exhibiting making of the beneficial effect of statins in BMD because of the poor glycemic control due to type 2 diabetes (page 2865, col. 1, last paragraph). Patients suffering from type 2 diabetes are not necessarily the same patients suffering from bone loss and/or requiring bone repair. As such, Applicant's arguments are not on point.

Regarding 16), the fact that the disclosure of Parhami et al., (2002) teaches two inhibitors of HMG-CoA reductase, i.e., mevastatin and mevinolin, that suppress expression and activity of

ALP, a key enzyme involved in differentiation and mineralization of osteoblastic cells and thus formation of a mineralized matrix (Parhami, page 1999, Fig. 1-osteocalcin expression (OC)), is not disputed. However, just because Applicants found that mevastatin inhibits mineralization of osteoblastic cells does not means that statins do not promote calcium mineral deposition. The art as a whole teaches that statins enhancing bone formation. Garrett et al., summarizes the role of statins at the time the invention was made, enhancing bone formation (Garrett et al., Feb. 2002, *Arthritis Res*, pp. 237-240). Note that the test for obviousness under 35 U.S.C. 103 requires a highly fact-dependent analysis involving taking the claimed subject matter as a whole and comparing it to the prior art. Like statins, side-chain oxysterols are HMG-CoA reductase inhibitors. Consequently, based on the teachings in the prior art as a whole, one would expect that like statins treatment enhances bone growth and differentiation of osteo-progenitor human cells, side-chain oxysterols would also be promoting bone formation.

Provisional Rejection, Obviousness Type Double Patenting-

Claims 1, 3, 6, 8, 11, 12, 15-17, 19-21, 23-26 and 28 remain provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-3, 5-9, 11-15, 17-20, 22-25 and 27-30 of copending Application No. 10,569,994, in view of Paralkar et al., 20040176423 (Date of Publication September 9, 2004), for the reasons already of record as set forth in the office action of 06-11-2008.

Applicants have not properly address the specific grounds of rejection as set forth in the previous office action of 12/09/2009.

Claims 1, 3, 6, 8, 11, 12, 15-17, 19-21, 23-26 and 28 remain provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-11 of copending Application No. 11/918,089 and over claims 1-9 and 15 of the copending Application No. 11/991,322, for the reasons already of record as set forth in the office action of 06-11-2008.

Applicants have not properly address the specific grounds of rejection as set forth in the previous office action of 12/09/2009.

New grounds of objection/rejection

New Grounds of Rejection

Claim Rejections - 35 USC § 112- Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 15-17 and 19-21, 23-26 and 28 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. **This is a new rejection necessitated by amendment of the claims in the response filed on 04-09-2010.**

Claim 15 is indefinite in its recitation of "induce differentiation of MSCs into osteoblasts, thereby increasing increase the number of osteoblasts present in bone tissue". It is unclear whether the administration to the patient induces differentiation of MSCs or increases the number of osteoblasts, or there is a grammatical error in the sentence. As such the metes and bounds of the claim cannot be determined.

For the purpose of a compact prosecution the claims have been interpreted as increasing the number of osteoblasts.

Additionally claims 15 and 19 recite, "suffering from bone loss and/or requiring bone repair". It is unclear what the metes and bounds of this term, as "and" could be interpreted to include only suffering from bone loss, or suffering from bone loss and requiring bone repair, or, "or" would imply that the treatment of a patient is in the alternative. Appropriate correction is required.

Claims 16 and 17 are indefinite insofar as they depend from claim 15.

Claims 20, 21, 23-26 and 28 are also included in the rejection as they directly or indirectly depend on claim 19.

Claim Rejections - 35 USC § 112- First paragraph- New Matter

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 15-17 and 19-21, 23-26 and 28 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. **This is a new rejection necessitated by amendment of the claims in the response filed on 04-09-2010.**

Claim 15 has been amended to recite "a method of treating a patient from bone loss and/or requiring bone repair comprising … to induce differentiation of MSCs into osteoblasts, thereby increasing the number of osteoblasts present in bone tissue". Likewise, **claim 19** recites "a method of treating a patient from bone loss and/or requiring bone repair comprising administering to the patient at least one oxysterol".

The response dated 04-09-2010 does not indicate where support may be found for the above limitations regarding treating a patient from bone loss and/or requiring bone repair and inducing differentiation of MSCs into osteoblasts, thereby increasing the number of osteoblasts present in bone tissue. A review of the specification as filed reveals no specific disclosure of regarding treating a patient from bone loss and/or requiring bone repair and inducing differentiation of MSCs into osteoblasts, thereby increasing the number of osteoblasts present in bone tissue. What the specification does disclose regarding enhancing bone formation and/or enhancing bone repair is the administration of agents to a patient which influence the differentiation of MSC into osteoblasts by systemic delivery or localized treatment (¶ [0017] (¶ [0046] ,¶ [0048] of the published application). There is nothing more to lead one of skill in the art to appreciate that of treating a patient from bone loss and/or requiring bone repair comprising … to induce differentiation of MSCs into osteoblasts, thereby increasing the number of osteoblasts present in bone tissue was a part of the invention, as opposed to a administration to a patient to increase the differentiation of marrow stromal cells into osteoblasts or to increase the number of osteoblasts present in bone tissue (original claim 15). Hence, is not clear that the Applicant was in possession of a genus of undefined "methods of treating a patient from bone loss and/or requiring bone repair comprising … to induce differentiation of MSCs into

osteoblasts, thereby increasing the number of osteoblasts present in bone tissue" at the time of filing.

Claims 15-17 and 19-21, 23-26 and 28 will remain rejected until Applicant cancels all new matter.

Conclusion

Claims 1-3, 6-8, 11-17, 19-21, 23-26 and 28 are rejected.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maria Leavitt whose telephone number is 571-272-1085. The examiner can normally be reached on M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach, Ph.D can be reached on (571) 272-0739. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group Art Unit 1633; Central Fax No. (571) 273-8300. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Maria Leavitt/

Maria Leavitt
Primary Examiner, Art Unit 1633